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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
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09/540,342 10/18/97

1582/0705

EXAMINER

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ART UNIT PAPER NUMBER

1819

11

DATE MAILED: 07/18/97

This is a communication from the examiner in charge of your application.  
COMMISSIONER OF PATENTS AND TRADEMARKS

### OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on 2/25/97 & 4/14/97

☐ This action is FINAL.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

#### Disposition of Claims

- ☒ Claim(s) 1, 4, 5, 8, 10-15, 18-28, & 33-50 is/are pending in the application.  
Of the above, claim(s) \_\_\_\_\_ is/are withdrawn from consideration.  
☐ Claim(s) \_\_\_\_\_ is/are allowed.  
☒ Claim(s) 1, 4, 5, 8, 10-15, 18-28 & 33-50 is/are rejected.  
☐ Claim(s) \_\_\_\_\_ is/are objected to.  
☐ Claim(s) \_\_\_\_\_ are subject to restriction or election requirement.

#### Application Papers

- ☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.  
☐ The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.  
☐ The proposed drawing correction, filed on \_\_\_\_\_ is ☐ approved ☐ disapproved.  
☐ The specification is objected to by the Examiner.  
☐ The oath or declaration is objected to by the Examiner.

#### Priority under 35 U.S.C. § 119

- ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).  
☐ All ☐ Some\* ☐ None of the CERTIFIED copies of the priority documents have been  
☐ received.  
☐ received in Application No. (Series Code/Serial Number) \_\_\_\_\_  
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\*Certified copies not received: \_\_\_\_\_

- ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

#### Attachment(s)

- ☐ Notice of Reference Cited, PTO-892  
☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 10  
☐ Interview Summary, PTO-413  
☒ Notice of Draftsperson's Patent Drawing Review, PTO-948  
☐ Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

Serial Number 08/540,343  
Art Unit 1819

The Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1819.

Claims 2, 3, 6, 7, 9, 16, and 17 are cancelled, claims 1, 4, 5, 8, 10-15, and 18-27 are amended, and new claim 33 has been added, as requested in the amendment filed 2/25/97. New claims 34-50 have been added as requested in the supplemental amendment filed 4/14/97. Claims 1, 4, 5, 8, 10-15, 18-28 and 33-50 are now in the application.

Claims 1, 4, 5, 8, 10-12, 28, 34-39 are newly rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Newly amended claims 1 and 34 recite a method for potentiating "the response" of a tumor cell, but do not identify the nature of "the response" which is potentiated, so that it is unclear what are the metes and bounds of the claimed invention.

Claim 28 is indefinite because it recites a process employing an adenovirus, but it depends on claim 24, which states that the virus is HSV.

The specification remains objected to under 35 U.S.C. § 112, first paragraph, as failing to adequately teach how to use the claimed invention, for the reasons discussed below and in the last office action.

Newly amended claims 1 and 34 recite a method for potentiating "the response" of a tumor cell, which encompasses any response; however, the only response disclosed by the specification which is potentiated by injection of HSV-1 into mouse having a tumor formed from implanted glioblastoma cells (Example 1), or by injection of an adenovirus into a tumor formed

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from colon carcinoma cell implanted in a mouse which is subsequently treated by radiation therapy (Example 2), is inhibition of tumor growth. One skilled in the art at the time the application was filed would have recognized that the art of reliably eliciting a given response from any type of tumor cell is highly unpredictable as discussed in the previous office action. Said skilled artisan would have recognized that the response of any tumor cell to any anti-tumor agent depends critically and unpredictably on the chemical structure of the anti-tumor agent and on the type of tumor cell. When the anti-tumor agent is a nucleic acid vector and the tumor cells are growing in vivo, so that the method is a form of gene therapy, the successful operation of the method is also recognized to depend unpredictably on the means by which the nucleic acid vector is administered to the subject, also as discussed in the previous office action. The specification is deficient in its teachings regarding the method wherein injection of HSV-1 into a mouse with a tumor formed from implanted glioblastoma cells, because nowhere in the disclosed example does the specification teach the site or mode of injection, i.e. intravenous, intraperitoneal, subcutaneous, etc., so that it is unclear to one skilled in the art how to effectively administer the HSV-1 to obtain the disclosed results.

Claims 1, 8, 10-13, 18-23, and 25-27 recite any herpesvirus, and claims 4, 14, and 24, recite any herpes simplex virus (HSV). One skilled in the art would recognize that there are many diverse types of herpesvirus, such as Epstein-Barr virus and cytomegalovirus, and that the structures and activities of herpesviruses within the HSV family also show clear and distinct differences. Said skilled artisan would reasonably have considered that, in the absence of data regarding the specific features of herpesviruses in general, and of HSV viruses in particular, which mediate the inhibition of glioblastoma tumor

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cell proliferation, it is unpredictable and uncertain whether any virus other than HSV-1 will have the anti-glioblastoma tumor activity of HSV-1 as disclosed in Example 1. Similarly, claims 28 and 34-50 recite any type of adenovirus, yet one skilled in the art would recognize that the different types of adenoviruses also differ concretely in their structures and activities, and one skilled in the art at the time the application was filed would reasonably have considered that it is unpredictable and uncertain whether any virus other than HSV-1 will have the anti-colon carcinoma tumor activity of adenovirus type 5 as disclosed in Example 2.

Given the breadth of the claims, which encompass potentiation of an unspecified type of response in a wide variety of different type of tumor cells by a wide variety of different types of herpesviruses and adenoviruses, given the unpredictability of the successful operation of the claimed invention, and given the lack of guidance in the specification or in the prior art regarding how to use the claimed invention successfully in all but one of its narrowest embodiment wherein the method comprises the steps of direct injection of a type 5 adenovirus into a colon carcinoma tumor, followed by X-irradiation, undue experimentation would have been required by one skilled in the art at the time the application was filed to practice the claimed invention.

Claims 1, 4, 5, 8, 10-15, 18-28 and 33-50 remain rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification, as stated in the last office action for claims .

The rejection of claims 1, 8, 12, 23-25, and 27 under 35 U.S.C. § 102(b) as anticipated by Fujiwara et al. has been withdrawn in view of the amendments filed 2/25/97 and 4/14/97.

The rejection of claims 1, 4, 5, 8, 10-15, 18-2 under 35 U.S.C. § 103 as obvious over Wills et al. taken with additional

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references has been withdrawn in view of the amendments filed 2/25/97 and 4/14/97.

The claims are allowable over the prior art because at the time the application was filed the prior art did not teach or suggest the claimed methods in a manner such that one of ordinary skill in the art would have reasonably expected to be able to make or use the claimed invention successfully.

No claims are allowed.

Applicant's arguments filed 2/25/97 and 4/14/97 have been fully considered but they are not deemed to be persuasive.

Applicants urge that objection to the specification and rejection of the claims under 35 U.S.C. § 112, first paragraph, for failure to adequately teach how to use the invention, be reconsidered and withdrawn, because the disclosed examples adequately teach one skilled in the art how to use the claimed methods wherein herpesviruses or adenoviruses are administered as anti-cancer agents to inhibit tumor growth.

The examiner maintains that the rejection of the claims under 35 U.S.C. 112, first paragraph, in the first office action was based on reference to relevant teachings in the published literature, and on consideration of the nature of the invention, the quantity of experimentation required, the amount of guidance presented in the specification, the presence and absence of working examples, the state of the prior art, the degree of predictability of successful operation of the claimed invention, and the breadth of the claims, as called for in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). The objections to the specification and rejection of claims have been partially withdrawn in response to Applicants' amendments; however, the claims still encompass non-enabled methods wherein any type of

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herpesvirus or adenovirus is administered by any means to any of a wide variety of tumors. 35 U.S.C. 112, first paragraph, requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art. Fisher, 166 USPQ at 21-22, 24 (CCPA 1970). The disclosed examples only support narrow embodiments of the claimed invention, as discussed above. Accordingly, rejection of the broadly claimed methods under 35 U.S.C. 112, first paragraph, is proper.

Applicant's amendment necessitated the new grounds of rejection. Accordingly, **THIS ACTION IS MADE FINAL**. See M.P.E.P. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

General Information Regarding Further Correspondence

Any inquiry concerning this or earlier communications from the examiner should be directed to Dr. Charles Rories, Group 1800, Art Unit 1819, at telephone number (703)-308-1120. The examiner can normally be reached from 7:30 AM to 5:00 PM on Monday-Thursday and alternate Fridays.


If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jasmine Chambers, can be reached at (703)-308-2035.

Papers related to this application may be submitted to Art Unit 1819 in Crystal Mall I by facsimile transmission to telephone number (703)-308-0294. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG (November 15, 1989).

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Any inquiry of a general nature or relating to the status of this application, should be directed to the Group 1800 receptionist, at telephone number (703)-308-0196.

7 July 1997

  
Charles C. P. Rories  
Patent Examiner  
Art Unit 1819